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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,452	09/01/2004	Tadao Ohno	P25874	7197

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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
10/22/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/505,452	OHNO ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *24 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-4,6-12 and 16-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4, 6-12, 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Amendment filed August 24, 2007 in response to the Office Action of February 27, 2007 is acknowledged and has been entered. Previously pending claims 5 and 13-15 have been cancelled, claims 1-2 have been amended. Claims 1-4, 6-12, 16-19 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4, 6-12, 16-19 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 27, 2007, Section 1, page 2.

Applicant argues that the claims are enabled by the specification because the specification clearly conveys how to obtain the soluble ingredients claimed and thus clearly conveys how to make the claimed immunoadjuvant.

The argument has been considered but has not been found persuasive because although the specification clearly teaches general extraction techniques, it does not teach how to predictably distinguish between those extracts that will function as immunoadjuvants and those that will not and given the clear teaching of Barot-Ciorbaru et al, the invention as currently claimed is not enabled.

Applicant argues that it appears that the Office may believe that not all soluble fractions derived from a cell or tissue will result in immunomodulatory activity, however Applicant's note that the claims do not require that each element of the recited soluble fraction exhibit an immunomodulatory activity and all that the claims require is the formation of an immunoadjuvant prepared according to the claimed steps.

The argument has been considered but has not been found persuasive for the reasons set forth above. Further, it is noted for Applicant's information that the finding that not all soluble fractions derived from a cell or tissue will result in immunodulatory activity is not based solely on a "belief" of the Examiner but is based on the objective findings of those of skill in the art as exemplified by the clear teachings of Barot-Cirobaru et al. Further, although the claims do not require that each element of the recited soluble fraction exhibit an immunomodulatory activity and all that is required is the formation of an immunoadjuvant prepared according to the claimed steps, Barot-Ciorbaru et al clearly teach that not every bacterial extract is a source of immunostimulatory substances and that only certain soluble extracts possess immunomodulatory activity. Although the claims are now drawn to extracts derived by multiple methods, neither the claims nor the specification as originally filed teaches how to predictably distinguish between those extracts that will function as immunoadjuvants and those that will not and given the clear teaching of Barot-Ciorbaru et al, the invention as currently claimed is not enabled.

Applicant argues that the action fails to show that a "soluble ingredient....removed by washing with an organic solvent and/or hot water" would necessarily not result in an immunoadjuvant. The argument has been considered

but has not been found persuasive because given the teaching of Barot-Ciorbaru et al that not all extracts comprise immunostimulatory activity, it could not be predicted, nor would it be expected that all extracts would have immunostimulatory activity, regardless of the method of extraction and given that neither the claims nor the specification teaches how to predictably distinguish between those extracts that have immunostimulatory activity and those that do not, the invention as currently claimed is not enabled.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-4, 6-12, 16-19 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed February 27, 2007, Section 1, page 2.

Applicant argues that Ohno et al do not teach vaccines with tumor material immobilized to an adjuvant and that Ravindernath et al do not suggest a use for an adjuvant alone without being attached to a whole cell and to suggest that one of skill in the art would immobilize a bacterial adjuvant taught by Ravindernath et al

without a whole cell affixed thereto – to anything – is to ignore the totality of the disclosure of Ravindernath et al.

The argument has been considered but has not been found persuasive because Applicant is arguing the references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which made up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination. In re Young, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In re Keller 642 F.2d 413,208 USPQ 871 (CCPA 1981).

Applicant further argues that a person of skill in the art would not replace the whole cell of Ravindernath et al with a formalin fixed (or any otherwise solidified) cell from Ohno with any expectation of success because (a) Ravindernath et al emphases the importance of whole cells because tumor-associated antigens do not need to be first identified or purified, omitting the purification step wherein any extraction method that removes the tumor antigen from the membrane environment is likely to alter its immunogenic properties, (b) Ravindernath et al teachings a general method of conjugating cell surface-associated adjuvants to any available membrane component.

The argument has been considered but has not been found persuasive because although the microparticles of Ohno et al are not whole cells, the microparticles of Ohno et al clearly do not require either the identification or purification of tumor antigens to function as claimed. Further, since the antigens are not purified or extracted, but remain *in situ* in the particles, it is clear, given

that the particles would necessarily comprise membrane fragments, that the antigens would not be removed from the membrane environment and the immunogenic properties of the antigens would not be expected to altered and given that Examiner takes note that methods of conjugating cell surface associated adjuvants were conventional in the art at the time the invention was made, given the know immunogenic properties of MPLtaught by Ravindermath et al the claimed invention is obvious over the combined references and one would have a reasonable expectation of successfully producing the claimed tumor vaccine/immunoadjuvant.

Applicant argues that since the formalin fixed cells are no longer capable of living in cell culture, there would be no expectation of success in conjugating the adjuvant to the tumor microparticles of Ohno et al. The argument has been considered but has not been found persuasive because conjugation of adjuvants was conventional in the art at the time the invention was made.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

Finally, for Applicant's information, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S._, 82, USPQ2d 1385 (2007), that ".....[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results" (KSR, 550 U.S. at_, 82 USPQ2d at 1395). The court further found that "..... the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious" (KSR, 550 U.S. at_, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of

known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions" ((KSR, 550 U.S. at_, 82 USPQ2d at 1396).

Finally, for Applicant' information, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S._, 82, USPQ2d 1385 (2007), that "a person of ordinary skill attempting to solve a problem will" not " be led only to those elements of prior art designed to solve the same problem....." (KSR, 550 U.S. at_, 82 USPQ2d at 1397). The court found that "When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variant, 35 USC 103 likely bars its patentability" (KSR, 550 U.S. at_, 82 USPQ2d at 1396). Further the court found that the Federal Circuit has erred in applying the teaching-suggestion-motivation test in an overly rigid and formalistic way, in particular by concluding "that a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try'" (KSR, 550 U.S. at_, 82 USPQ2d at 1397) and has further determined that ".....[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results" (KSR, 550 U.S. at_, 82 USPQ2d at 1395). The court further found that "..... the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious" (KSR, 550 U.S. at_, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements

according to their established functions" ((KSR, 550 U.S. at_, 82 USPQ2d at 1396).

Given the above, applying the same logic to the instant process claims, it would have been *prima facie* obvious to modify the method of Ohno et al to produce a tumor vaccine comprising tumor microparticles conjugated to MPL because Ohno specifically recognizes the problem of increasing the efficacy of tumor vaccines with adjuvants including bacterial derivatives and Ravindemath et al specifically teaches that MPL is a known bacterial adjuvant which elicits immune responses against tumor antigens and prolongs survival. Given the known problem to be solved, given the known and conventional bacterial adjuvant, given that conventional and successful techniques for conjugating bacterial adjuvants were known in the art at the time the invention ion was made, given the successful therapeutic efficacy of conjugation of MPL to a moiety that did not have defined tumor antigens, given that at least a subset of the tumor antigens of Ohno et al would be expected to retain their in situ structure, the variation of the technique of Ravindemath et al to conjugate the known adjuvant to the known microparticles for the production of a tumor vaccine for the treatment of tumor, is obvious.

Finally, given the above, the claimed invention is obvious over the prior art because it would have been obvious to try the known methods of conjugation of bacterial adjuvants to conjugate MPL to the tumor microparticles for the making the claimed tumor vaccine with a reasonable expectation of success wherein the instantly claimed invention is simple a predictable variant of the invention of Ohno et al in combination with Ravindemath et al, wherein the success of the solution to the problem would be a product of ordinary skill and common sense but not the product of innovation.

8. All other objections and rejections set forth in the previous Office Action are hereby withdrawn.

9. No claims allowed.

10. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

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11. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

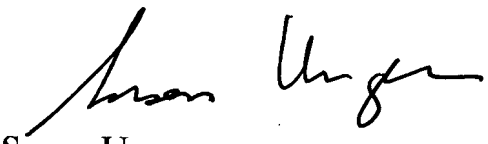
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF

THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar
Primary Patent Examiner
October 11, 2007